

REMARKS/ARGUMENTS

With this amendment, claims 1, 5-6, 8, 9, 42-45, and 53 are pending. Claims 7, 19, 23-29, 33-41, 46-52, and 54-80 are withdrawn. Claims 10-18, 20-22, and 30-32 are cancelled. For convenience, the Examiner's rejections are addressed in the order presented in n October 19, 2006, Office Action.

I. Status of the claims

Claims 1 and 42 are amended to recite an ADNF peptide of SEQ ID NO:1 that has all D-amino acids. Support for this amendment is found throughout the specification, for example, at page 3, lines 20-30. original claim 4, and original claim 45. These amendments add no new matter.

II. Claim objections

As requested in the Office Action, claims 46-52 are marked as withdrawn or withdrawn-currently amended. Claims 46-52 depend from claim 42 and Applicants maintain their right to rejoinder of the claims after allowance of claim 42.

III. Rejections under 35 U.S.C. §103(a)

The Office Action maintains rejections of claims 1-6, 8-9, 42-45, and 49-53 as allegedly obvious over Brennenman (US Patent No. 6,174,862), Voet *et al.* (1995) and Goodman (US Patent No. 4,587,046). The present Office Action also Rozhavskaya-Arena *et al.* *Endocrinology* 141:2501-2507 (2000) as representative of the state of the art at the time of filing. In response to the arguments of the previous response, the Office Action alleges that Goodman *et al.* does not teach away from using D-amino acids.

First, Applicants assert that Rozhavskaya-Arena *et al.* was incorrectly cited as prior art. Rozhavskaya-Arena *et al.* was published in July 2000. The present application claims priority to a provisional application filed on August 18, 1999, *i.e.*, USSN 60/149,956 (the '956 application). The '956 application discloses the claimed invention at, *e.g.*, The experiments that

form the basis of the claimed invention, including, *e.g.*, in vitro experiments using cerebral cortical cells and animal model systems, are disclosed in the '956 application at, *e.g.*, the examples section pages 41-47, and the Figures and Figure legends.

Applicants also provide, as Exhibit A, a declaration from inventor Dr. Illana Gozes to demonstrate that the biological activity of the all D-amino acid peptides was unexpected. A reference, Guptasarma, *FEBS* 310:205-210 (1992), also provides evidence of the unexpected effect and is submitted as Exhibit C. (Although the declaration indicates that Guptasarma is Exhibit D, it is indeed submitted as Exhibit C.)

According to Dr. Gozes, the all D-amino acid ADNF I and ADNF III peptides were synthesized to serve as negative controls. Based on the model for the structure of all D-amino acid peptide put forth in Guptasarma, all D-amino acid peptides are not believed to have the biological activity of the related all L-amino acid peptides. According to Dr. Gozes the cited references do not disclose an all D-amino acid peptide that has biological activity. In fact, the authors of the Rozhavskaya-Arena *et al.* references used an all D-amino acid leptin peptide as an inactive, negative control. Thus, the cited references are not sufficient to provide a reasonable expectation for success in generating an all D-amino acid peptide with biological activity. Moreover, Dr. Gozes indicates that the biological activity of the D-amino acid ADNF I and ADNF III polypeptides was unexpected. Thus, this combination of references does not render the claimed invention obvious.

In view of the above amendments and evidence, withdrawal of the rejections for alleged obviousness is respectfully requested.

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Examining Group 1649

PATENT

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,


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